Danger in the jungle

Bell, Samira; Selby, Nicholas M.; Bagshaw, Sean M.

Published in:
Kidney International

DOI:
10.1016/j.kint.2019.11.020

Publication date:
2020

Danger in the Jungle: Sensible Care to Reduce Avoidable Acute Kidney Injury in Hospitalized Children

Samira Bell[1]
Nicholas M. Selby[2]
Sean M. Bagshaw[3]

1. Division of Population Health and Genomics, University of Dundee, Dundee, UK.
2. Centre for Kidney Research and Innovation, Division of Medical Sciences and Graduate Entry Medicine, University of Nottingham, UK
3. Department of Critical Care Medicine, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, Canada

Running title:

Word count: 1166

Corresponding author:
Sean M. Bagshaw, MD, MSc, FRCPC
Department of Critical Care Medicine,
Faculty of Medicine and Dentistry and School of Public Health
University of Alberta
2-124E Clinical Sciences Building
8440-112 St NW Edmonton, T6G2B7 CANADA
Email: bagshaw@ualberta.ca

ABSTRACT:

When children require hospital admission, many receive medications with nephrotoxic potential. As such, this can translate into an increased risk of acute kidney injury. In this context, acute kidney injury is hospital acquired, often iatrogenic, and portends risk of adverse outcomes. The Nephrotoxic Injury Negated by Just-in-Time Action study implemented a multicenter hospital-wide quality improvement initiative to detect and reduce nephrotoxin exposure in children aimed at decreasing the rates of potentially avoidable acute kidney injury. This commentary explores the findings and implications of the Nephrotoxic Injury Negated by Just-in-Time Action study

KEY WORDS: quality, safety, nephrotoxin, acute kidney injury, implementation

EDITORIAL:

“It is foolish to be convinced without evidence, but it is equally foolish to refuse to be convinced by real evidence.”

Upton Sinclair, author of “The Jungle”

The delivery of acute medical care in hospital settings is complex and often associated with substantial risk of medical errors and adverse events.[1]

The rate of adverse events among adult hospitalized patients has been estimated at 7.5 events per 100 hospitalizations, of which close to 2 in 5 were adjudicated as being avoidable.[2] In hospitalized children, the rate of adverse events approaches 10%, is more common among academic centers and less often deemed to be preventable.[3]

Acute kidney injury (AKI) is no exception to these observations. AKI can often be considered an iatrogenic hospital-acquired condition and has been shown to be associated with short-term complications including higher mortality, longer hospital stay, incremental costs and downstream risk of chronic kidney disease (CKD).[4] Indeed, hospital-acquired AKI is currently being considered as a quality indicator of harm by the Centers for Medicare and Medicaid Services.[5]

Drugs with nephrotoxic potential are commonly prescribed for hospitalized children and are often a necessity; however, their administration is associated with risk of iatrogenic AKI.[6] Nephrotoxin-induced AKI in turn is associated with greater risk of death, prolonged hospitalization and costs. This risk can be mitigated, in part, by enhanced monitoring of children perceived to be at greater risk leveraged through wide-scale implementation of electronic health records.[7] Many children, by virtue of their disease and treatments, may inherently be at greater risk of AKI; however, these children can also be readily identified.[8] As such, there should be little tolerance for potentially avoidable episodes of AKI that occur in hospitalized children.

In this issue, Goldstein and colleagues present the multi-center Nephrotoxic Injury Negated by Just-in time Action (NINJA) program[9], extending their prior work that reduced avoidable AKI episodes by 62% in a single US center.[8] NINJA engaged nine diverse children's hospitals across the United States to implement hospital-wide (non-ICU) screening (i.e., "trigger tool") for nephrotoxin exposure. This was defined as receipt of an aminoglycoside for three or more days or three or more nephrotoxin medications (from a defined list) on the same calendar day. The program involved an inter-professional two-day learning session, integrated bundled intervention aimed to mitigate nephrotoxin exposure including a medication review (medication substitution if feasible) and obtaining a daily serum creatinine during exposure. The program aimed to reduce AKI, defined as an increase in serum creatinine of 50% within seven days or 0.3 mg/dL (26.5 µmol/L) within 48 hours following initial exposure. The primary endpoint was the number of exposed children with AKI per 1000 non-critically ill patient-hospital days. This was complemented by several additional process and outcomes measures. A statistical change in the primary outcome was conservatively estimated by observing eight consecutive bi-weekly rates in the same direction either above or below the

baseline rate, and further confirmed using autoregressive integrated moving average (ARIMA) modeling.

The NINJA program was effectively and sustainably implemented across nine institutions; however, as expected, there was variation in time to maturity and reporting. Overall, there was a 23.8% reduction in the rates of AKI (change from 1.7 to 1.3 AKI episodes per 1000 patient hospital days) and AKI rates per exposure (36.7% reduction), despite variable rates of nephrotoxin exposures over the >600,000 hospital-days observed. The program estimated 242 episodes of AKI were avoided with program implementation over the 2-year study, assuming the baseline rates of AKI would have persisted. These reductions in AKI rates are particularly notable bearing in mind the intervention required increased testing of serum creatinine, which could have resulted in ascertainment bias leading to an apparent increase in AKI rates.[10] Indeed, this phenomenon is a well-recognized early step in quality improvement. This was observed in some of the centres, after which AKI rates fell as the intervention became more embedded demonstrating that initiatives focused on improving quality of care for children at risk of AKI can improve outcomes. The lack of serum creatinine testing at baseline in children at risk further highlights that suboptimal AKI care remains common in routine clinical practice.

The authors are to be congratulated on their successful delivery of a multicentre quality improvement project, which itself is a considerable achievement. The NINJA program also nicely highlights some of challenges in performing such a study. Firstly, there was variation between centres. Individual sites varied in their observed reduction in AKI rates following implementation of the intervention, largely contingent on their baseline rates. Three sites with low baseline AKI rates relative to post-implementation rates showed no further reduction; whereas those with higher baseline rates showed improvement. In addition, the effectiveness of complex interventions may have some dependency on the local context in which they are introduced - there are examples of AKI bundles appearing to work in some settings but not others.[10] Correspondingly, some flexibility was required in implementing the intervention across different centres (e.g., the method for the trigger tool). As expected with a hospital-wide approach, it was difficult to achieve 100% compliance in all aspects of the intervention across all centres. Despite this, benefits were still seen, and it remains uncertain as to whether even larger gains would have been seen with greater uptake and in settings with higher baseline AKI rates. These observations reinforce how quality improvement initiatives, such as NINJA, necessitate a careful appreciation of local culture with concomitant evaluation of the barriers and/or facilitators of successful implementation, and an approach to monitor and report these. Another consideration is the sheer spectrum of medications associated with altered kidney function, and our relative under-appreciation of their

synergistic potential to contribute to AKI. This may represent a yet to be explored source of variation in the observed reduction in AKI rates.

Some additional questions arise from these results. To date, quality improvement initiatives such as NINJA have focused on short-term outcomes. However, we could speculate that a reduction in rates of AKI, avoidance of more severe AKI and/or shortening of AKI duration may translate into future reduced mortality or lower incidence of downstream CKD. This remains to be investigated in future studies with longer follow-up. In addition, whilst is it logical that the NINJA intervention should be applicable to all populations at risk of AKI, it has not yet been tested in adult populations to demonstrate its wider generalizability. Moreover, following a change in practice, it is important to consider potential unintended consequences arising as a result of the intervention (e.g. increased rates of sepsis associated with alternative choices in antibiotics).

The findings of NINJA strongly suggest that a clinically meaningful proportion of nephrotoxin-related AKI events are avoidable, children at risk can be readily identified and that a relatively simple intervention can translate into substantial reductions in unnecessary harm. NINJA also reinforces how the EHR can be leveraged to trigger alerts that identify children at risk of AKI and to potentially intervene to mitigate preventable episodes of AKI. Applying this new knowledge may help hospitalised children navigate a “safer” jungle.

DISCLOSURES:

Dr. Bagshaw is supported by a Canada Research Chair in Critical Care Nephrology. Dr. Bagshaw reports receiving consulting fees from Baxter Healthcare Inc., CNA Diagnostics Inc. All the other authors declared no competing interests.

REFERENCES:

1. Institute of Medicine Committee on Quality of Health Care in America, ed. To Err Is Human. Washinton, D.C.: National Academies Press; 1999.
2. Baker GR, Norton PG, Flintoft V, et al. The Canadian Adverse Events Study: the incidence of adverse events among hospital patients in Canada. CMAJ 2004;170:1678-86.
3. Matlow AG, Baker GR, Flintoft V, et al. Adverse events among children in Canadian hospitals: the Canadian Paediatric Adverse Events Study. CMAJ 2012;184:E709-18.
4. Menon S, Kirkendall ES, Nguyen H, Goldstein SL. Acute kidney injury associated with high nephrotoxic medication exposure leads to chronic kidney disease after 6 months. J Pediatr 2014;165:522-7 e2.

5. Measures Inventory Tool: Hospital Harm - Acute Kidney Injury (eCQM). Centers for Medicare & Medicaid Services (CMS),, 2019. 2019, at https://cmit.cms.gov/CMIT_public/ViewMeasure?MeasureId=5904.)
6. Moffett BS, Goldstein SL. Acute kidney injury and increasing nephrotoxic-medication exposure in noncritically-ill children. Clin J Am Soc Nephrol 2011;6:856-63.
7. Selby NM, Casula A, Lamming L, et al. An Organizational-Level Program of Intervention for AKI: A Pragmatic Stepped Wedge Cluster Randomized Trial. J Am Soc Nephrol 2019;30:505-15.
8. Goldstein SL, Kirkendall E, Nguyen H, et al. Electronic health record identification of nephrotoxin exposure and associated acute kidney injury. Pediatrics 2013;132:e756-67.
9. Goldstein SL, Dahale DS, Kirkendall ES, et al. Nephrotoxic Acute Kidney Injury Reduction in Hospitalized Children: A Prospective Multi-Center Quality Improvement Initiative. Kidney International 2019.
10. Kolhe NV, Reilly T, Leung J, et al. A simple care bundle for use in acute kidney injury: a propensity score-matched cohort study. Nephrol Dial Transplant 2016;31:1846-54.